

ACIP

Feb. 21-22, 2007

Guillain-Barré Syndrome (GBS) Among Recipients of Meningococcal Conjugate Vaccine (MCV4, Menactra®) Update Oct. 2006-Jan. 2007

Robert L. Davis, MD, MPH

Director

Immunization Safety Office

Office of the Chief Science Officer

Centers for Disease Control and Prevention



SAFER • HEALTHIER • PEOPLE™



Outline

- Update on surveillance for GBS following MCV4
 - Vaccine Adverse Event Reporting System (VAERS)
 - Vaccine Safety Datalink (VSD)
- Observed compared to expected rate calculations
- Age and season stratified analyses
- Discussion and limitations



GBS after MCV4 Vaccination: Background

- GBS is a rapidly evolving polyradiculoneuropathy generally manifest as a symmetric motor paralysis
- MMWR reports reviewed GBS cases following receipt of Menactra®
 - October 2005: 5 cases reported to VAERS
 - April 2006: 3 additional cases reported to VAERS
 - October 2006: 9 additional GBS cases reported to VAERS



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: Background

- Two new cases since last MMWR through January 2007: total of 19 GBS cases <6 wks after MCV4 vaccination reported to VAERS
- There were also 4 confirmed reports of GBS in 13-19 year olds with onset intervals > 6 weeks; these are not included in further analyses



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: July 2005 – Jan 2007

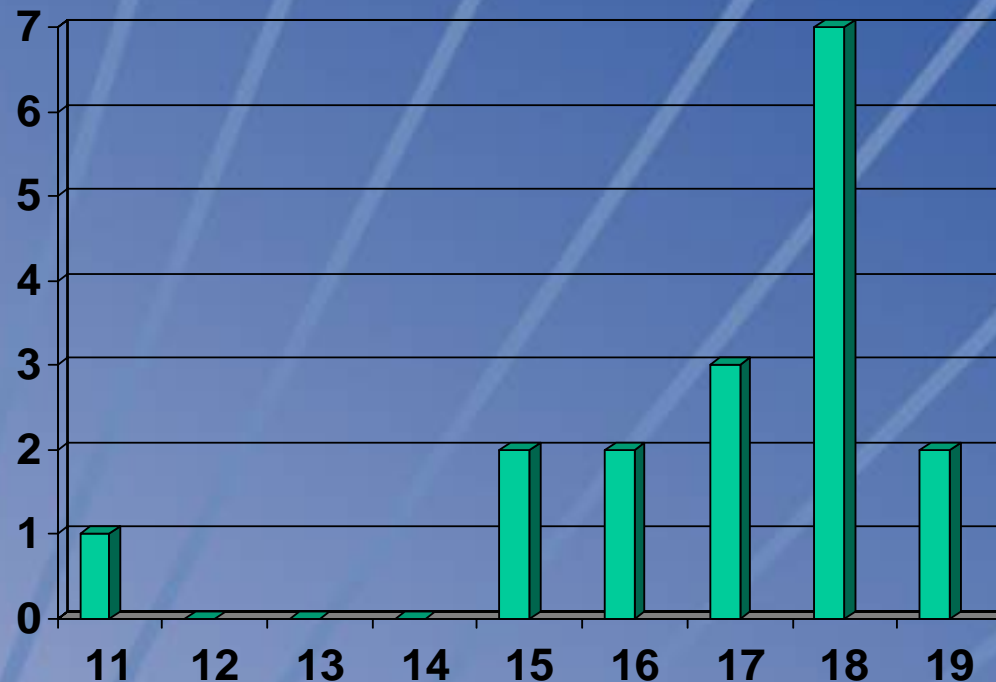
- A total of 19 cases of GBS after Menactra vaccine with:
 - Onset interval of 2-33 days.
 - Of these, 17 were 11-19 years old
- Information from MCOs within the VSD indicated that ~94% of MCV4 recipients were 11–19 year olds



SAFER • HEALTHIER • PEOPLE™



Number of GBS Reports to VAERS within 6 weeks of MCV4 Administration, by Age



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: Data from VSD

- VSD Rapid Cycle Project from April 2006 through January 2007:
 - 156,542 doses administered
 - **Zero** cases GBS observed among vaccine recipients 11–19 years old within 6 weeks of vaccination
 - 0-1 cases were expected



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: Observed vs. Expected

Was the observed reporting rate (RR) for GBS after MCV4 vaccination in VAERS higher than expected?

- VAERS Observed = 1.78 cases per million person-months

Calculation:

*6.93 million vaccine doses distributed to 11–19 year olds =
9.57 million person-months (6.93* 6 weeks follow-up per
dose)*

17 observed cases /9.57 million person-months



SAFER • HEALTHIER • PEOPLE™



Observed (VAERS)/ expected

- Expected (using HCUP 2000-2003) =
1.13 per million person-months (11-19 y/o)
 - Observed/expected = $1.78/1.13 = 1.57$
(95% CI = .94 – 2.45)
- Expected (using VSD 2000-2004) =
1.11 per million person-months (11-19 y/o)
 - Observed/expected = $1.78/1.11 = 1.59$
(95% CI = .90 – 2.67)



GBS after MCV4 Vaccination: Public Health Impact

- If these data accurately represent the true magnitude of increased risk after MCV4 vaccination, then:
- 0.89 excess cases/ million doses (CI = 0.015 – 5.39)
-

Calculation:

Number of excess cases of GBS/1 million doses distributed to 11–19 year olds:

(Observed - Expected)/ 6.93 million doses

(17 – 10.8)/ 6.93 million doses



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: Rates by Age

- Among 11-14 year olds in VSD
 - Number doses = 3.0 million (4.2 million person-months)
 - Expected Background rate GBS = 1.0 case/million person-months (= 4.2 cases)
 - Observed in VAERS= 1 case
 - Observed/expected ratio= 1.0 / 4.2
 - **Rate ratio = 0.25 (.01 – 1.20) – Controlling for Season**
- Among 15-19 year olds in VSD
 - Number doses = 3.9 million (5.4 million person-months)
 - Expected background rate GBS = 1.2 case/million person-months (= 6.5 cases)
 - Observed in VAERS = 16 cases
 - Observed/expected ratio = 16/6.5
 - **Rate ratio = 2.48 (1.30 – 4.55) – Controlling for Season**



GBS after MCV4 Vaccination: Discussion

- For 11-19 Year Olds, there is no statistically significant evidence of an increased risk of GBS after MCV4 vaccination.
- Although there appears to be a small increased risk for GBS after MCV4 vaccination in the 15-19 year old age category, the inherent limitations of VAERS require that these findings be viewed with caution
- Substantial uncertainty exists regarding the risk estimate, using either the HCUP or VSD background incidence rate
- Timing of neurologic symptoms within 1–5 weeks of vaccination among reported cases is of concern



SAFER • HEALTHIER • PEOPLE™



GBS after MCV4 Vaccination: Limitations

- Completeness of GBS reporting to VAERS is unknown
 - Under-reporting of GBS after MCV4 vaccination would raise the risk estimates
 - No surge in GBS reports to VAERS after any MMWR; expected if underreporting were marked
- VSD has limited ability to detect rare adverse events
 - Not finding any GBS after MCV4 vaccination in 11-19 year olds does not offer substantial reassurance regarding MCV4 safety



GBS after MCV4 Vaccination: Discussion

- A larger study is necessary to provide a more definitive assessment
 - A larger study led by Harvard Pilgrim has begun; data regarding the risk for GBS following MCV4 is expected in approximately 2 years
 - The study period is necessary to accumulate cases and attain sufficient statistical power
- Ongoing evaluation of GBS after MCV4 vaccination is being performed using VSD



Acknowledgments

- Elaine Miller
- Eric Weintraub
- Claudia Vellozzi
- John Iskander
- VSD Principal Investigators
- CDC and FDA VAERS Teams



SAFER • HEALTHIER • PEOPLE™

